

**BEST AVAILABLE COPY****REMARKS**

Claims 1, 2, 4-11, 14, 15, and 21-29 are pending in the application. Claims 14 and 29 have been amended. Claims 14 and 29 have been amended to better define the invention and to distinguish over claims 1, 10, 13, and 15 of copending Application No. 09/186,810. Claims 14 and 29 are in the group of claims which are provisionally rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over a group of claims which includes claims 1, 8, 10, 13, and 15 of copending Application No. 09/186,810. Support for the amendment to claims 14 and 29 is found at page 4, line 15-17, where covalent bonding is contrasted with specific binding interactions for binding the polypeptide growth factor to the tissue. Covalent bonding is further distinguished from specific binding interactions at page 14, lines 9-16, wherein it is stated, "Chemical binding includes, for example, covalent bonding, a plurality of noncovalent chemical interactions or both covalent and noncovalent interactions. Noncovalent chemical interactions include, for example, hydrogen bonding, van der Waals interactions and molecular rearrangements, which characterize, for example, antibody-antigen, specific binding protein-receptor and enzyme-substrate associations." Applicants respectfully assert that no new matter has been added and request reconsideration of the claims currently pending in the application.

**I. Status of Examiner's Consideration of Applicants' Information Disclosure Statement**

The Examiner's acknowledgement of the Applicants' PTO-1449 form submitted with the communication filed on May 24, 2004 is noted with appreciation. The Continuation Sheet (PTOL-303) of the Advisory Action mailed July 23, 2004 indicates

"The initialed PTO-1449 for the May 24, 2004 IDS is attached." However, this document was not included in the mailing. Applicants' representative respectfully requests that the Examiner forward the initialed PTO-1449 form in the next Office communication.

## II. Rejection under the judicially created doctrine of obvious-type double patenting

On page 2 of the Office Action, claims 1, 2, 9, 14, 21, and 29 are provisionally rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 1, 8, 10, 13, 15, 34-35, and 38-40 of copending Application No. 09/186,810.

Applicants submit that claims 1, 2, 9, 14, 21, and 29 of the present application are distinct and independently patentable from the claims of copending Application Number 09/186,810. Claims 1, 2, 9, and 29 are directed to a prosthesis for a human patient comprising allograft or xenograft tissue having a polypeptide growth factor associated therewith, and claims 14 and 21 are directed to a prosthetic heart valve comprising a substrate with associated VEGF. They are independently patentable from claims 1, 8, 10, 13, 15, 34, 35, and 38-40 of copending Application No. 09/186,810. In particular, claims 14 and 29 have been amended to exclude covalent bonding using crosslinking agents, which is one of the methods for associating the substrate and polypeptide growth factor in claims 1, 8, 10, 13, and 15 of copending Application No. 09/186,810 in order to further distinguish the subject matter of claims 14 and 29 from the claims of copending Application No. 09/186,810. Also, since this is a provisional rejection, Applicants will consider filing a terminal disclaimer complying with 37 CFR

3.73(b) when these claims or the allegedly conflicting claims of the copending application are found to be allowable and the rejection is no longer a provisional one. Reconsideration is respectfully requested.

### III. Rejection under 35 U.S.C. §102 (b)

A. On page 3 of the Office Action, claims 25 and 28 are rejected under 35 U.S.C. §102 (b) as being anticipated by Cahalan, et al. (U.S. Patent No. 5,308,641).

Applicants respectfully traverse the rejections.

Cahalan, et al. do not disclose crosslinked natural tissue having an exogenous polypeptide growth factor associated therewith. Cahalan, et al teach the use of a polyalkylimine spacer to attach a biomolecule to a solid surface. Crosslinking agents are used to crosslink the polyalkylimine spacer, not natural tissue in a prosthesis. Cahalan's teaching of spacers and their uses, along with the recitation of lightly crosslinking the attached polyalkylimine spacer with glutaraldehyde crosslinkers, does not anticipate Applicants' crosslinked tissue associated with an exogenous polypeptide growth factor.

To anticipate a claim, the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Therefore, all claim elements, and their limitations, must be found in the prior art reference to maintain

a rejection based on 35 U.S.C. §102. Applicants respectfully submit that the teaching of Cahalan, et al. of attaching a molecule to a surface by making use of a polyalkylimine spacer does not anticipate associating an exogenous polypeptide growth factor with a crosslinked natural tissue.

Dependent claim 28, which is dependent from independent claim 25, was also rejected under 35 U.S.C. §102(b) as being anticipated by Cahalan, et al. While Applicants do not acquiesce with the particular rejections to the dependent claim, it is believed that these rejections are moot in view of the remarks made in connection with independent claim 25. Claim 28 includes all of the limitations of the base claim and recites additional features which further distinguish it from the cited reference. Therefore, dependent claim 28 is also in condition for allowance.

Applicants respectfully request withdrawal of the rejection of claims 25 and 28 under 35 U.S.C. §102 (b) as being anticipated by Cahalan, et al.

B. On page 4 of the Office Action, claims 25 and 26 are rejected under 35 U.S.C. §102 (b) as being anticipated by Bayne, et al. (EP 0 476 983). Applicants respectfully request reconsideration.

Bayne, et al. do not disclose associating an exogenous polypeptide growth factor with crosslinked natural tissue in a prosthesis, as claimed by Applicants.

Bayne, et al. teach two embodiments for the coverage of artificial blood vessels with vascular endothelial cells. The first embodiment involves the growing of cells in vitro on culture medium in the presence of VEGF II and then plating the cells on the inside surface of a synthetic polymeric blood vessel. The second embodiment involves

coating artificial tubular supports in vitro with VEGF II prior to implantation into a patient. Following implantation, endothelial cells grow on the surface of the synthetic polymeric blood vessel. Bayne, et al. do not disclose associating an exogenous polypeptide growth factor with the crosslinked natural tissue of a prosthesis. Since Bayne, et al. do not disclose every element of the claimed invention, the reference does not anticipate claim 25.

Claim 26 depends from claim 25 and therefore incorporates all the limitations of claim 25 and is also not anticipated by Bayne, et al.

Applicants respectfully request withdrawal of the rejection of claims 25 and 26 under 35 U.S.C. §102 (b) as being anticipated by Bayne, et al.

#### IV. Rejection under 35 U.S.C. § 103(a)

A. Claims 25 and 26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bayne, et al. alone. The Examiner asserts that if the tubular supports coated with VEGF II do not include umbilical cord vein, then it would have been obvious to use umbilical vein as the tubular support. However, the only mention of umbilical cord vein is in connection with the first embodiment discussed above, that is, the in vitro growth of cells in culture in the presence of VEGF II. The second embodiment, coating in vitro with VEGF II prior to implantation into a patient, is directed solely to tubular supports, referred to (page 8, lines 20-21) as artificial surfaces.

Applicants respectfully traverse the rejection, since the reference does not suggest associating an exogenous polypeptide growth factor with a crosslinked natural

tissue making up a prosthesis. In fact, the reference teaches away from the use of natural tissues in conjunction with exogenous polypeptide growth factors.

Dependent claim 26, which is dependent from independent claim 25, was also rejected under 35 U.S.C. §103(a) as being unpatentable over Bayne, et al. While Applicants do not acquiesce with the particular rejections to the dependent claim, it is believed that these rejections are moot in view of the remarks made in connection with independent claim 25. Claim 26 includes all of the limitations of the base claim and recites additional features which further distinguish the claim from the cited reference. Therefore, dependent claim 26 is also in condition for allowance.

Applicants respectfully request that the rejection of claims 25 and 26 over Bayne, et al. under 35 U.S.C. §103(a) be withdrawn.

B. On page 4 of the Office Action, claims 1, 2, 4, 5, 9-11, and 29 are rejected as being unpatentable over Bayne, et al. in view of Wadström (U.S. Patent No. 5,631,011). The Examiner cited Wadström to show that fibrin is a common biologic tissue adhesive.

Applicants respectfully traverse the rejections.

The deficiencies in Bayne, et al. have been discussed above. These deficiencies are not supplied by Wadström, as Wadström also does not teach, suggest, or motivate association of a polypeptide growth factor with tissue. Wadström only teaches how to improve fibrin glue so that it does not have a low viscosity problem and also teaches how such an improved glue promotes wound healing without scar formation or development of adhesions. There is no motivation to combine the teaching of Bayne, et al. with that of Wadström. The combined teaching does not suggest the invention of

independent claims 1 and 29, since Bayne, et al. is directed to coating of VEGF II on artificial surfaces and not tissues and Wadström does not suggest otherwise. Therefore, claims 1 and 29 are not obvious based on Bayne, et al. in view of Wadström.

Claims 2, 4-5, and 9-11 are dependent from claim 1. While Applicants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with Independent claim 1. These dependent claims include all of the limitations of the base claim and any intervening claims, and recite additional features which further distinguish these claims from the cited references. Therefore, dependent claims 2, 4-5 and 9-11 are also in condition for allowance.

Applicants respectfully request the withdrawal of the rejection of claims 1, 2, 4, 5, 9-11, and 29 as being unpatentable over Bayne, et al., in view of Wadström.

C. On page 5 of the Office Action, claims 6-8, 14, 15, 21-24, and 27-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bayne, et al. and Wadström further in view of Carpentier, et al. (U.S. Patent No. 4,648,881). The Examiner admits that Bayne, et al. do not disclose uncrosslinked tissue, the heart valve form of the tissue, or the other tissue types as claimed. However, the Examiner states that Carpentier, et al. teach that all uncrosslinked and crosslinked forms of tissue, heart valve tissue forms and other types of tissue are well known in the art.

Applicants respectfully traverse the rejections.

The discussion above for claims 1-2, 4-5, 9-11, and 29 with regard to Bayne, et al. and Wadström also applies here. Bayne, et al. not only do not disclose

uncrosslinked tissue, the heart valve form of the tissue, or the other tissue types as claimed, Bayne, et al. also do not disclose the association of growth factors with tissues at all, as noted above, crosslinked or uncrosslinked. Therefore, the deficiency in Bayne, et al. is not just that uncrosslinked tissue, the heart valve form of the tissue, or the other tissue types as claimed are not disclosed or taught, but that no association of growth factors with tissue of any kind is disclosed or taught. Wadström does not supply the deficiency, and the disclosure in Carpentier, et al. of tissue calcification does not motivate one of ordinary skill in the art to arrive at the invention of claims 6-8, 14, 27, and 28. Since the deficiency of Bayne, et al. is not supplied by Wadström in view of Carpentier, et al. without using Applicants' invention as a road map, there is no teaching or motivation in the cited references to guide one of ordinary skill in the art to arrive at the invention of claims 6-8, 14, 27, and 28.

Claims 15 and 21-24 are dependent from independent claim 14 and were also rejected under 35 U.S.C. §103(a) as being unpatentable over Bayne, et al. and Wadström further in view of Carpentier, et al. While Applicants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with independent claim 14. These dependent claims include all of the limitations of the base claim and any intervening claims, and recite additional features which further distinguish these claims from the cited references. Therefore, dependent claims 15 and 21-24 are also in condition for allowance.



Applicants respectfully request withdrawal of the rejection of claims 6-8, 14, 15, 21-24, 27, and 28 under 35 U.S.C. § 103(a) as being unpatentable over Bayne, et al. and Wadström further in view of Carpentier, et al.

#### V. Conclusion

In view of the amendments and reasons provided above, it is believed that all pending claims are in condition for allowance. Applicants respectfully request favorable reconsideration and early allowance of all pending claims.


If a telephone conference would be helpful in resolving any issues concerning this communication, please contact Applicants' attorney of record, Hallie A. Finucane at (952) 253-4134.

Respectfully submitted,

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